

SEQUENCE LISTING

<110> SCHMIDT, Harald
ZABEL, Ulrike
POLLER, Wolfgang

<120> Isolated and Purified Human Soluble
Guanylylcyclase alpha 1/beta 1 (hsGCalpha1/beta 1)

<130> VOS-101

<140> US 09/762,767

<141> 2001-02-13

<150> PCT/DE99/02601

<151> 1999-08-16

<150> DE 198 37 015.6

<151> 1998-08-14

<160> 10

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 3015

<212> DNA

<213> genomic DNA

<400> 1

```
cccttatggc gattgggagg ctgcagagac caggactcag ttcccctgcc ctagtctgag 60
cctagtgggt gggactcagc tcagagtcag tttccagaa gcaggtttca gtgcagagtt 120
ttcctacact tttcctgcgc tagagcagcg agcagcctgg aacagaccca ggcggaggac 180
acctgtgggg gagggagcgc ctggaggagc ttagagaccc cagccgggag tgatctcacc 240
atgtgcggat ttgcgaggcg cgccctggag ctgctagaga tccggaagca cagccccgag 300
gtgtgcgaag ccaccaagac tgcggctctt ggagaaagcg tgagcagggg gccaccgcgg 360
tctccgcgcc tgtctgcacc ctgtgccttg agctgcctga cagtgacaat gacatcccag 420
ttaccagtgt ccttgaattg atagtggctt ctgtttgtca gtctcatata agaactacag 480
ctcatcagga ggagatcgca gcagggttaag agacaccaac accatgttct gcacgaagct 540
caaggatctc aagatcacag gagagtgtcc tttctcctta ctggcaccag gtcaagttcc 600
taacgagtct tcagaggagg cagcaggaag ctccagagagc tgcaaagcaa cagtgcctat 660
ctgtcaagac attcctgaga agaacatata agaaagtctt cctcaaagaa aaaccagtcg 720
gagccgagtc tatcttcaca ctttggcaga gagtatttgc aaactgattt tcccagagtt 780
tgaacggctg aatgttgac ttccagagaa attggcaaag caaaaataa aagaaagcag 840
gaaatctttg gaaagagaag actttgaaaa aacaattgca gagcaagcag ttgcagcagg 900
agttccagtg gaggttatca aagaatctct tgggtgaagag gtttttaaaa tatgttacga 960
ggaagatgaa aacatccttg ggggtggttg aggcaccctt aaagattttt taaacagctt 1020
cagtaccctt ctgaaacaga gcagccattg ccaagaagca ggaaaaaggg gcaggcttga 1080
ggagcctcc attctatgcc tggataagga ggatgatttt ctacatgttt actacttctt 1140
ccctaagaga accacctccc tgattcttcc cgcatcata aaggcagctg ctacagttat 1200
atatgaaacg gaagtggag tgctgttaat gcctccctgc ttccataatg attgcagcga 1260
gtttgtgaat cagccctact tgtgttactc cgttcacatg aaaagcacca agccatccct 1320
```

```

gtccccagc aaacccagc cctcgctggt gattcccaca tcgctattct gcaagacatt 1380
tccattccat ttcattgttg acaaagatat gacaattctg caatttggca atggcatcag 1440
aaggctgatg aacaggagag actttcaagg aaagcctaatt tttgaagaat actttgaaat 1500
tctgactcca aaaatcaacc agacgttttag cgggatcatg actatgttga atatgcagtt 1560
tggtgtacga gtgaggagat gggacaactc tgtgaagaaa tcttcaaggg ttatggacct 1620
caaaggccaa atgatctaca ttgttgaatc cagtgcatac ttgttttttg ggtcacccctg 1680
tgtggacaga ttagaagatt ttacaggacg agggctctac ctctcagaca tcccaattca 1740
caatgcactg agggatgttg tcttaatagg ggaacaagcc cgagctcaag atggcctgaa 1800
gaagaggctg gggaaagctga aggtaccct tgagcaagcc caccaagccc tggaggagga 1860
gaagaaaaag acagtagacc ttctgtgctc catatttccc tgtgagggtg ctccagcagct 1920
gtggcaaggg caagttgtgc aagccaagaa gttcagtaat gtcaccatgc tcttctcaga 1980
catcgttggg ttcactgcca tctgctccca gtgctcaccg ctgcaggcca tcaccatgct 2040
caatgcactg tacactcgct tcgaccagca gtgtggagag ctggatgtct acaaggtgga 2100
gaccattggc gatgcctatt gtgtagctgg gggattacac aaagagagtg atactcatgc 2160
tggtcagata gcgctgatgg cctgaagat gatggagctc tctgatgaag ttatgtctcc 2220
ccatggagaa cctatcaaga tgcgaattgg actgcactct ggatcagttt ttgctggcgt 2280
cggtggagtt aaaatgcccc gttactgtct ttttggaac aatgtcactc tggctaacaa 2340
atttgagtc tgcagtgtac cagcaaaaat caatgtcagc ccaacaactt acagattact 2400
caaagactgt cctggtttcg tgtttacccc tcgatcaagg gaggaacttc caccaaactt 2460
ccctagttaa atccccgaa tctgccattt tctggatgct taccaacaag gaacaaactc 2520
aaaacatgc ttccaaaaga aagatgtgga agatggcaat gccaattttt taggcaaagc 2580
atcaggaata gattagcaac ctatatacct atttataagt ctttgggggt tgactcattg 2640
aagatgtgta gagcctctga aagcacttta gggattgtag atggctaaca agcagtatta 2700
aaatttcagg agccaagtca caatctttct cctgtttaac atgacaaaat gtactcactt 2760
cagtacttca gctcttcaag aaaaaaaaaa aaaccttaaa aagctacttt tgtgggagta 2820
tttctattat ataaccagca cttactacct gtactcaaaa ttcagcacct tgtacatata 2880
tcagataatt gtagtcaatt gtacaaactg atggagtcac ctgcaatctc atatcctggg 2940
ggaatgccat gggtattaaa gtgtgtttgt gatagtgtcg tcaaaaaaaaaa aaaaaaaaaa 3000
aaaaaaaaaa aaaaaa 3015

```

<210> 2

<211> 690

<212> PRT

<213> human soluble guanylyl cyclase a1 (hsGCal))

<400> 2

```

Met Phe Cys Thr Lys Leu Lys Asp Leu Lys Ile Thr Gly Glu Cys Pro
 1             5             10            15
Phe Ser Leu Leu Ala Pro Gly Gln Val Pro Asn Glu Ser Ser Glu Glu
 20            25            30
Ala Ala Gly Ser Ser Glu Ser Cys Lys Ala Thr Val Pro Ile Cys Gln
 35            40            45
Asp Ile Pro Glu Lys Asn Ile Gln Glu Ser Leu Pro Gln Arg Lys Thr
 50            55            60
Ser Arg Ser Arg Val Tyr Leu His Thr Leu Ala Glu Ser Ile Cys Lys
 65            70            75            80
Leu Ile Phe Pro Glu Phe Glu Arg Leu Asn Val Ala Leu Gln Arg Thr
 85            90            95
Leu Ala Lys His Lys Ile Lys Glu Ser Arg Lys Ser Leu Glu Arg Glu
100           105           110
Asp Phe Glu Lys Thr Ile Ala Glu Gln Ala Val Ala Ala Gly Val Pro
115           120           125
Val Glu Val Ile Lys Glu Ser Leu Gly Glu Glu Val Phe Lys Ile Cys
130           135           140
Tyr Glu Glu Asp Glu Asn Ile Leu Gly Val Val Gly Gly Thr Leu Lys

```

145	Asp	Phe	Leu	Asn	Ser	Phe	Ser	Thr	Leu	Leu	Lys	Gln	Ser	Ser	His	Cys
					165						170				175	
	Gln	Glu	Ala	Gly	Lys	Arg	Gly	Arg	Leu	Glu	Asp	Ala	Ser	Ile	Leu	Cys
				180						185					190	
	Leu	Asp	Lys	Glu	Asp	Asp	Phe	Leu	His	Val	Tyr	Tyr	Phe	Phe	Pro	Lys
			195					200					205			
	Arg	Thr	Thr	Ser	Leu	Ile	Leu	Pro	Gly	Ile	Ile	Lys	Ala	Ala	Ala	His
		210				215						220				
	Val	Leu	Tyr	Glu	Thr	Glu	Val	Glu	Val	Ser	Leu	Met	Pro	Pro	Cys	Phe
225						230					235				240	
	His	Asn	Asp	Cys	Ser	Glu	Phe	Val	Asn	Gln	Pro	Tyr	Leu	Leu	Tyr	Ser
				245						250					255	
	Val	His	Met	Lys	Ser	Thr	Lys	Pro	Ser	Leu	Ser	Pro	Ser	Lys	Pro	Gln
			260						265					270		
	Ser	Ser	Leu	Val	Ile	Pro	Thr	Ser	Leu	Phe	Cys	Lys	Thr	Phe	Pro	Phe
			275				280						285			
	His	Phe	Met	Phe	Asp	Lys	Asp	Met	Thr	Ile	Leu	Gln	Phe	Gly	Asn	Gly
		290				295						300				
	Ile	Arg	Arg	Leu	Met	Asn	Arg	Arg	Asp	Phe	Gln	Gly	Lys	Pro	Asn	Phe
305						310					315				320	
	Glu	Glu	Tyr	Phe	Glu	Ile	Leu	Thr	Pro	Lys	Ile	Asn	Gln	Thr	Phe	Ser
				325						330					335	
	Gly	Ile	Met	Thr	Met	Leu	Asn	Met	Gln	Phe	Val	Val	Arg	Val	Arg	Arg
			340						345					350		
	Trp	Asp	Asn	Ser	Val	Lys	Lys	Ser	Ser	Arg	Val	Met	Asp	Leu	Lys	Gly
		355					360						365			
	Gln	Met	Ile	Tyr	Ile	Val	Glu	Ser	Ser	Ala	Ile	Leu	Phe	Leu	Gly	Ser
370						375					380					
	Pro	Cys	Val	Asp	Arg	Leu	Glu	Asp	Phe	Thr	Gly	Arg	Gly	Leu	Tyr	Leu
385						390					395				400	
	Ser	Asp	Ile	Pro	Ile	His	Asn	Ala	Leu	Arg	Asp	Val	Val	Leu	Ile	Gly
				405						410					415	
	Glu	Gln	Ala	Arg	Ala	Gln	Asp	Gly	Leu	Lys	Lys	Arg	Leu	Gly	Lys	Leu
			420						425					430		
	Lys	Ala	Thr	Leu	Glu	Gln	Ala	His	Gln	Ala	Leu	Glu	Glu	Glu	Lys	Lys
			435				440						445			
	Lys	Thr	Val	Asp	Leu	Leu	Cys	Ser	Ile	Phe	Pro	Cys	Glu	Val	Ala	Gln
		450				455						460				
	Gln	Leu	Trp	Gln	Gly	Gln	Val	Val	Gln	Ala	Lys	Lys	Phe	Ser	Asn	Val
465						470					475				480	
	Thr	Met	Leu	Phe	Ser	Asp	Ile	Val	Gly	Phe	Thr	Ala	Ile	Cys	Ser	Gln
				485					490					495		
	Cys	Ser	Pro	Leu	Gln	Val	Ile	Thr	Met	Leu	Asn	Ala	Leu	Tyr	Thr	Arg
			500						505					510		
	Phe	Asp	Gln	Gln	Cys	Gly	Glu	Leu	Asp	Val	Tyr	Lys	Val	Glu	Thr	Ile
		515						520					525			
	Gly	Asp	Ala	Tyr	Cys	Val	Ala	Gly	Gly	Leu	His	Lys	Glu	Ser	Asp	Thr
530						535						540				
	His	Ala	Val	Gln	Ile	Ala	Leu	Met	Ala	Leu	Lys	Met	Met	Glu	Leu	Ser
545						550					555				560	
	Asp	Glu	Val	Met	Ser	Pro	His	Gly	Glu	Pro	Ile	Lys	Met	Arg	Ile	Gly
				565					570						575	
	Leu	His	Ser	Gly	Ser	Val	Phe	Ala	Gly	Val	Val	Gly	Val	Lys	Met	Pro
			580						585					590		

Arg Tyr Cys Leu Phe Gly Asn Asn Val Thr Leu Ala Asn Lys Phe Glu
 595 600 605
 Ser Cys Ser Val Pro Arg Lys Ile Asn Val Ser Pro Thr Thr Tyr Arg
 610 615 620
 Leu Leu Lys Asp Cys Pro Gly Phe Val Phe Thr Pro Arg Ser Arg Glu
 625 630 635 640
 Glu Leu Pro Pro Asn Phe Pro Ser Glu Ile Pro Gly Ile Cys His Phe
 645 650 655
 Leu Asp Ala Tyr Gln Gln Gly Thr Asn Ser Lys Pro Cys Phe Gln Lys
 660 665 670
 Lys Asp Val Glu Asp Gly Asn Ala Asn Phe Leu Gly Lys Ala Ser Gly
 675 680 685
 Ile Asp
 690

<210> 3
 <211> 2443
 <212> DNA
 <213> genomic DNA

<400> 3
 ccccccccg ccgtgccgc ctctgcctgg gtcccttcgg ccgtacctct gcgtgggggc 60
 tgctcccccg gctcccggtg cagacacccat gtacggattt gtgaatcacg ccctggagtt 120
 gctggtgatc cgcaattacg gccccgaggt gtgggaagac atcaaaaaag aggcacagtt 180
 agatgaagaa ggacagtttc ttgtcagaat aatatatgat gactccaaaa cttatgattt 240
 gggtgctgct gcaagcaaag tctcaatct caatgctgga gaaatcctcc aaatgtttgg 300
 gaagatgttt ttcgtctttt gccagaatc tggttatgat acaatcttgc gtgtcctggg 360
 ctctaattgtc agagaatttc tacagaacct tgatgctctg caccgaccacc ttgctaccat 420
 ctaccagga atgcgtgcac ctcccttttag gtgcactgat gcagaaaagg gcaaaggact 480
 cattttgcac tactactcag agagagaagg acttcaggat attgtcattg gaatcatcaa 540
 aacagtggca caacaaatcc atggcactga aatagacatg aagggttatc agcaaagaaa 600
 tgaagaatgt gatcactac aatttttaat tgaagaaaaa gaggtaaaag aagaggattt 660
 ttatgaagat cttgacagat ttgaagaaaa tggtagccag gaatcacgca tcagcccata 720
 tacattctgc aaagcttttc cttttcatat aatatttgac cgggacctag tggtagctca 780
 gtgtggcaat gctatataca gagttctccc ccagctccag cctgggaatt gcagccttct 840
 gtctgtcttc tcgtgggttc gtccctcatat tgatattagt ttccatggga tcctttctca 900
 catcaatact gtttttgtat tgagaagcaa ggaaggattg ttggatgtgg agaaattaga 960
 atgtgaggat gaactgactg ggactgagat cagctgctta cgtctcaagg gtcaaattgat 1020
 ctacttacct gaagcagata gcatactttt tctatgttca ccaagtgtca tgaacctgga 1080
 cgatttgaca aggagagggc tgtatctaag tgacatccct ctgcatgatg ccacgcgcga 1140
 tcttggtctt ttgggagaac aatttagaga ggaatacaaa ctcacccaag aactggaaat 1200
 cctcactgac aggtacagc tcacgttaag agccctggaa gatgaaaaga aaaagacaga 1260
 cacattgctg tattctgtcc ttccctcgtc tgttgccaat gagctgcggc acaagcgtcc 1320
 agtgccctgcc aaaagatatg acaatgtgac catcctcttt agtggcattg tgggcttcaa 1380
 tgctttctgt agcaagcatg catctggaga aggagccatg aagatcgtca acctcctcaa 1440
 cgacctctac accagatttg acacactgac tgattcccgg aaaaacccat ttgtttataa 1500
 ggtggagact gttggtgaca agtatatgac agtgagtggg ttaccagagc catgcattca 1560
 ccatgcacga tccatctgcc acctggcctt ggacatgatg gaaattgctg gccaggttca 1620
 agtagatggg gaattctgtc agataacaat agggatacac actggagagg tagttacagg 1680
 tgtcatagga cagcggatgc ctcgatactg tctttttggg aatactgtca acctcacaag 1740
 ccgaacagaa accacaggag aaaagggaaa aataaatgtg tctgaatata catacagatg 1800
 tcttatgtct ccagaaaatt cagatccaca attccacttg gagcacagag gccagtgctc 1860
 catgaagggc aaaaaagaac caatgcaagt ttggtttcta tccagaaaaa atacaggaac 1920
 agaggaaaca aagcaggatg atgactgaat cttggattat ggggtgaaga ggagtacaga 1980

```

ctaggttcca gttttctcct aacacgtgcc aagcccagga gcagttcttc cctatggata 2040
cagattttct tttgtccttg tccattaccc caagactttc ttctagatat atctctcact 2100
atccgttatt caaccttagc tctgctttct attacttttt aggcttttagt atattatcta 2160
aagtttggtt tttgatgtgg atgatgtgag cttcatgtgt cttaaaatct actacaagca 2220
ttacctaaca tggatgatctg caagtagtag gcacccaata aatatttggt gaatttagtt 2280
aaatgaaact gaacagtgtt tggccatgtg tatatttata tcatgtttac caaatctggt 2340
tagtgttcca catatatgta tatgtatatt ttaatgacta taatgtaata aagtttatat 2400
catgttggtg tatatcatta tagaaatcat tttctaaagg agt 2443

```

```

<210> 4
<211> 619
<212> PRT
<213> (human soluble guanylyl cyclase b1 (hsGcb1))

```

```

<400> 4
Met Tyr Gly Phe Val Asn His Ala Leu Glu Leu Leu Val Ile Arg Asn
 1          5          10          15
Tyr Gly Pro Glu Val Trp Glu Asp Ile Lys Lys Glu Ala Gln Leu Asp
 20          25          30
Glu Glu Gly Gln Phe Leu Val Arg Ile Ile Tyr Asp Asp Ser Lys Thr
 35          40          45
Tyr Asp Leu Val Ala Ala Ala Ser Lys Val Leu Asn Leu Asn Ala Gly
 50          55          60
Glu Ile Leu Gln Met Phe Gly Lys Met Phe Phe Val Phe Cys Gln Glu
 65          70          75          80
Ser Gly Tyr Asp Thr Ile Leu Arg Val Leu Gly Ser Asn Val Arg Glu
 85          90          95
Phe Leu Gln Asn Leu Asp Ala Leu His Asp His Leu Ala Thr Ile Tyr
100          105          110
Pro Gly Met Arg Ala Pro Ser Phe Arg Cys Thr Asp Ala Glu Lys Gly
115          120          125
Lys Gly Leu Ile Leu His Tyr Tyr Ser Glu Arg Glu Gly Leu Gln Asp
130          135          140
Ile Val Ile Gly Ile Ile Lys Thr Val Ala Gln Gln Ile His Gly Thr
145          150          155          160
Glu Ile Asp Met Lys Val Ile Gln Gln Arg Asn Glu Glu Cys Asp His
165          170          175
Thr Gln Phe Leu Ile Glu Glu Lys Glu Ser Lys Glu Glu Asp Phe Tyr
180          185          190
Glu Asp Leu Asp Arg Phe Glu Glu Asn Gly Thr Gln Glu Ser Arg Ile
195          200          205
Ser Pro Tyr Thr Phe Cys Lys Ala Phe Pro Phe His Ile Ile Phe Asp
210          215          220
Arg Asp Leu Val Val Thr Gln Cys Gly Asn Ala Ile Tyr Arg Val Leu
225          230          235          240
Pro Gln Leu Gln Pro Gly Asn Cys Ser Leu Leu Ser Val Phe Ser Leu
245          250          255
Val Arg Pro His Ile Asp Ile Ser Phe His Gly Ile Leu Ser His Ile
260          265          270
Asn Thr Val Phe Val Leu Arg Ser Lys Glu Gly Leu Leu Asp Val Glu
275          280          285
Lys Leu Glu Cys Glu Asp Glu Leu Thr Gly Thr Glu Ile Ser Cys Leu
290          295          300
Arg Leu Lys Gly Gln Met Ile Tyr Leu Pro Glu Ala Asp Ser Ile Leu
305          310          315          320

```

```

Phe Leu Cys Ser Pro Ser Val Met Asn Leu Asp Asp Leu Thr Arg Arg
      325                      330                      335
Gly Leu Tyr Leu Ser Asp Ile Pro Leu His Asp Ala Thr Arg Asp Leu
      340                      345                      350
Val Leu Leu Gly Glu Gln Phe Arg Glu Glu Tyr Lys Leu Thr Gln Glu
      355                      360                      365
Leu Glu Ile Leu Thr Asp Arg Leu Gln Leu Thr Leu Arg Ala Leu Glu
      370                      375                      380
Asp Glu Lys Lys Lys Thr Asp Thr Leu Leu Tyr Ser Val Leu Pro Pro
385                      390                      395                      400
Ser Val Ala Asn Glu Leu Arg His Lys Arg Pro Val Pro Ala Lys Arg
      405                      410                      415
Tyr Asp Asn Val Thr Ile Leu Phe Ser Gly Ile Val Gly Phe Asn Ala
      420                      425                      430
Phe Cys Ser Lys His Ala Ser Gly Glu Gly Ala Met Lys Ile Val Asn
      435                      440                      445
Leu Leu Asn Asp Leu Tyr Thr Arg Phe Asp Thr Leu Thr Asp Ser Arg
      450                      455                      460
Lys Asn Pro Phe Val Tyr Lys Val Glu Thr Val Gly Asp Lys Tyr Met
465                      470                      475                      480
Thr Val Ser Gly Leu Pro Glu Pro Cys Ile His His Ala Arg Ser Ile
      485                      490                      495
Cys His Leu Ala Leu Asp Met Met Glu Ile Ala Gly Gln Val Gln Val
      500                      505                      510
Asp Gly Glu Ser Val Gln Ile Thr Ile Gly Ile His Thr Gly Glu Val
      515                      520                      525
Val Thr Gly Val Ile Gly Gln Arg Met Pro Arg Tyr Cys Leu Phe Gly
      530                      535                      540
Asn Thr Val Asn Leu Thr Ser Arg Thr Glu Thr Thr Gly Glu Lys Gly
545                      550                      555                      560
Lys Ile Asn Val Ser Glu Tyr Thr Tyr Arg Cys Leu Met Ser Pro Glu
      565                      570                      575
Asn Ser Asp Pro Gln Phe His Leu Glu His Arg Gly Pro Val Ser Met
      580                      585                      590
Lys Gly Lys Lys Glu Pro Met Gln Val Trp Phe Leu Ser Arg Lys Asn
      595                      600                      605
Thr Gly Thr Glu Glu Thr Lys Gln Asp Asp Asp
      610                      615

```

```

<210> 5
<211> 14
<212> PRT
<213> peptide (amino acids 634-647 of hsGCal)

```

```

<400> 5
Phe Thr Pro Arg Ser Arg Glu Glu Leu Pro Pro Asn Phe Pro
  1                      5                      10

```

```

<210> 6
<211> 22
<212> PRT
<213> peptide (amino acids 593-614 of hsGCb1)

```

<400> 6

Lys Gly Lys Lys Glu Pro Met Gln Val Trp Phe Leu Ser Arg Lys Asn
 1 5 10 15
 Thr Gly Thr Glu Glu Thr
 20

<210> 7

<211> 28

<212> DNA

<213> genomic DNA

<400> 7

aaaaggatcc atgttctgca cgaagctc

28

<210> 8

<211> 18

<212> DNA

<213> genomic DNA

<400> 8

attatggaag cagggagg

18

<210> 9

<211> 28

<212> DNA

<213> genomic DNA

<400> 9

aaaaggatcc atgtacggat ttgtgaat

28

<210> 10

<211> 20

<212> DNA

<213> genomic DNA

<400> 10

atgcgtgatt cctgggtacc

20